

Amendments to the Specification:

Please replace the text at page 13, from line 1 through line 16 with the following text:

--Figure 23 shows yeast two-hybrid assays to identify Smad interactors. Thirteen cDNAs identified in the screen were tested for interaction with Smad1 (Panel A); Smad2 (Panel B); Smad3 (Panel C); and DPC4 (Panel D).

Figure 24 shows yeast two-hybrid assays to identify the domain of Smad1 which interacts with HsN3. Panel A shows growth of HsN3 on Glucose-X-Gal plates; Panel B shows growth on Galactose-X-Gal Plates; Panel C shows a Western blot analysis of various yeast cell lysates using anti-LexA antibodies.

Figure 25 shows experiments examining the expression, processing and assembly of HsN3-containing complexes. Panel A shows results of an immunoprecipitation experiment. Immunoprecipitation of N<sub>3</sub>-F (lane 2) and HsN3 proteins lacking the prosequence (F-ΔN<sub>3</sub>) (lane 3) were carried out to provide a measure of the molecular weight of the processed form of N3-F. Panels B and C show results of immunoprecipitation experiments performed on COS cells transfected with N3-F (lanes 1), T7-Smad1 (lanes 4), Smad1C (lanes 5), or cotransfected with N3-F and T7-Smad1 (lanes 2), or N3-F and T7-Smad1C (lanes 3).

Figure 26 shows experiments examining the association of Smad1 with HsN3 relative to HsN3 assembly into proteasome complexes. COS cells were cotransfected with N3-F and T7-Smad1, or N3-F and T7-Smad2, and the lysates were first immunoprecipitated with anti-T7 antibody and then analyzed by Western blot with anti-Flag antibody (Panel A). Panel B shows specific coprecipitation of F-Smad1 with the prosequence-less HsN3 (T7-DN3).

Figure 27 shows experiments examining the effect of BMP type I receptor activation on Smad1 interaction with HsN3. Panel A shows results of an immunoprecipitation experiment performed using anti-T7 antibodies on COS cell extracts. Panel B shows results of a similar experiment, performed using anti-Flag antibodies.

Figure 28 shows experiments examining the localization of HsN3 and Smad1. Shown are confocal micrographs of untransfected (Panel A), Smad1 Overexpressing (Panel B), and Smad1 and ALK3Q233D overexpressing (Panel C) cells. COS cells were transfected with the wild-type BMP type I receptor, ALK3, the BMP type II receptor, and Smad1. Cells were treated with BMP7 (20 ng/ml) for either 30 mins (FIG. 28E), or 60 mins (FIG. 27F), and compared with untreated cells (FIG. 28D). Sub-Panels D1, E1 and F1 show HsN3 localization, Sub-panels D2,

E2 and F2 show Smad1 localization, and D3, E3, and F3 show colocalization of HsN3 and Smad1.

Figure 29 shows experiments examining the localization of HsN3 and Smad1. Panels A-D show representative confocal micrographs of COS cells overexpressing Smad1, HsN3 and ALK3Q233D in COS cells. Sub-Panels B1, C1 and D1 show HsN3 localization, Sub-panels B2, C2 and D2 show Smad1 localization, and Sub-Panels B3, C3 and D3 show co-localization of HsN3 and Smad1.

Figure 30 shows experiments examining the interaction of Smad1 interactors with antizyme. Interaction of the thirteen isolated clones with Antizyme (Panel A), and ODC (Panel B) are shown in a yeast two-hybrid assay.

Figure 31 shows experiments examining the proteasome-mediated degradation of SNIP1 (SEQ ID No. 3), (referred to in this figure as SMNI1). Panel A shows the nuclear localization of SNIP1 as determined by immunofluorescence. Panel B shows the interaction between SMNI-1 and Smad1, SMNI-1 and ATZ, SMNI-1 and HsN3, SMNI-1 and ODC, and ATZ and ODC. Panel C shows an alignment between SMNI-1 and the N-terminus of nipp N. Panel D shows results of a proteasome-mediated degradation of SMNI-1. The protein level of SNIP-1 in 100 ug of total protein lysate was determined by Western blot using anti-T7 monoclonal antibody, and equal loading was confirmed by Western blot using anti-a tubulin.

Figure 32 shows experiments examining the effect of proteasome inhibitors on TFG- $\beta$  family ligand activity. Top Panels A and B show the translocation of Smad1 from the cytoplasm to the nucleus upon OP- 1 treatment of sympathetic neurons. The middle Panels A-C and the lower Panel A show the concentration-dependent inhibition of dendrite formation upon exposure to lactacystin. Lower Panel B shows the time course of sensitivity to lactacystin with respect to the signaling pathway of OP-1--